

# **EXHIBIT**

# **T**

**IN THE UNITED STATES DISTRICT COURT  
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA  
CHARLESTON DIVISION**

<b>IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION</b> <hr/> <b>THIS DOCUMENT RELATES TO:</b>  <i>All Ethicon Wave 4 cases</i>	<b>Master File No. 2:12-MD-02327</b>  <b>MDL No. 2327</b>  <b>JOSEPH R. GOODWIN</b> <b>U.S. DISTRICT JUDGE</b>
--	---

**DECLARATION OF VLADIMIR V. IAKOVLEV, M.D., FRCPC, FCAP**

Vladimir V. Iakovlev declares:

1. I make this declaration in opposition to Defendants' motion to exclude certain opinions I have expressed in various Ethicon Wave 4 cases.
2. I am fully competent to make this declaration, and all statements made herein are based on my personal knowledge.
3. Defendants argue that my opinions are unreliable on the ground that I did not rely on a control specimen in performing my analysis of mesh explants from various plaintiffs.
4. I am aware that this Court has ruled that my opinions should be excluded "[t]o the extent that [I offer] complications opinions based on his examination of explanted mesh samples without the use of a control sample." *In re: Ethicon Inc. Pelvic Repair Sys. Prod. Liab. Litig.*, No. 2327, 2016 WL 4582228, at \*4 (S.D.W. Va. Sept. 1, 2016).
5. I respectfully submit that the Court's ruling is fundamentally at odds with the way in which pathologists make diagnoses. I regret that the record before the Court in 2016 did not afford the Court an accurate picture of how pathologists do their work, and I would like to

provide more information. The key fact is that pathologists do not use controls for diagnostic work. Doing so would make our work impossible as a practical matter.

#### **PATHOLOGY ROLE IN THE MEDICAL SCIENCES**

6. Pathology is not an isolated science, but rather a part of medicine as a whole. Originally, simple laboratory tests as well as autopsies were performed by the same physicians who would examine and treat their patients. Later, when the tests became more complex and time consuming, some physicians started specializing in performing these tests for other doctors, however the process of diagnostics and treatment remained the same – both the laboratory and the clinical physicians needed to understand medicine and diseases as a whole. Pathologists are fully trained physicians who later receive additional training in laboratory medicine. In their practice, they need to understand the clinical presentations, diagnostic approaches, and treatment strategies to interpret the laboratory tests and to focus on clinically relevant information.

7. One of the main textbooks used for training of pathology residents, and as an outline of Pathology Board examination, is “Robbins and Cotran Pathologic Basis of Disease”.

It states:

The four aspects of a disease process that form the core of pathology are its cause (etiology), the mechanisms of its development (pathogenesis), the biochemical and structural alterations induced in the cells and organs of the body (molecular and morphologic changes), and the functional consequences of these changes (clinical manifestations).

Kumar V, Abbas A, Fausto N, Aster J, Robbins and Cotran Pathological Basis of Disease, 8th Edition, Elsevier, Imprint: W.B. Saunders, 2010, Chapter 1, p.4.

8. As stated, using their knowledge of clinical medicine, normal anatomy, histology and pathology, pathologists complete the sequence: etiology-pathogenesis-morphological changes-clinical implications. The end target of this process is clinical implications while the morphological changes is the main tool of a pathologist. By definition, “changes” are the

features that are different from normal histology of unaffected healthy tissues. Pathologists use their knowledge of normal anatomy and histology (not controls) to detect the changes (abnormalities) and classify them as either the cause (etiology) or the result (disease):

Morphological changes refer to the structural alterations in cells or tissues that are either characteristic of a disease or diagnostic of an etiologic process.

*Id.*

9. Another fundamental textbook of Surgical pathology, Rosai and Ackerman's Surgical Pathology describes the role of a surgical pathologist:

The surgical pathologist not only must know his own field thoroughly, but he also must have a rich background in clinical medicine. He needs to understand the clinician's needs and respond to them accordingly. He must be in a position to advise the clinician about the biopsy or the excised material he receives.

He should be able to comment on whether additional therapy may be necessary and give information on the prognosis of the disease”.

J. Rosai, Rosai and Ackerman's Surgical Pathology, Mosby, 2004, p.3.

10. The process of correlating clinical manifestations with changes in the tissues, or clinico-pathological correlation has been the fundamental principle of studying and diagnosing the diseases:

Throughout its long history, pathology has been concerned with the study of the derangements of tissue structure and function that occur in disease, and the correlation of these changes with clinical signs and symptoms. This clinico-pathological approach, which pathology the foundation of clinical practice, remains as valid as ever.

R.C. Curran and J. Crocker,, Curran's Atlas of Histopathology, 4th edition,, Harvey Miller Publishers, Oxford University Press,, 2000,p.7.

11. I use the same approach in examining the mesh specimens. Deviations from normal histological range are detected and described (scarring, inflammation etc.). Then, based on the knowledge of established pathophysiological mechanisms, the changes are assessed if

they can explain the presenting symptoms. For example, observing mesh with scar tissue in the specimen would correlate with clinical descriptions of scarring around the mesh, sling tightening and urinary outflow obstruction attributed clinically to the mesh. However, finding a neoplasm (tumor) would not correlate and would override the clinical impression of a sling related urinary obstruction. In a reverse scenario, histological finding of a severe neuroma caused by the mesh would not explain pain in a distribution outside of the expected radiation pattern (back pain or pain in the lateral leg if the neuroma is seen in the vagina).

#### **USE OF CONTROLS IN PATHOLOGY**

##### **Diagnostic surgical pathology**

12. As described earlier, to make a diagnosis, pathologists use their knowledge of normal anatomy and histology to determine what is abnormal in the body. Obviously, there could not be a “control” body for an autopsy or thousands of normal samples for comparison to diagnose abnormalities in the surgical specimens and biopsies. Instead, pathologists use their knowledge of a normal range as a “control”. Pathology and medicine developed through descriptions of deviations from the learned normal range. The changes have been described and then related to the clinical symptoms or used to determine the cause of death. (This is the clinico-pathological approach discussed earlier.)

##### **Technical quality controls**

13. Physical tissue controls are still used in routine diagnostic pathology, but for specific purposes. These are quality controls for stains and other laboratory procedures. For example, samples of previously tested tissues are run together with the diagnostic samples to assure quality of the procedure. For some stains, the controls are included on the same slide as the diagnostic sample. Also, normal tissue components can be used as internal controls by

pathologists. For example, in mesh specimens, if normal tissue is included in a resection, staining quality can be checked examining the normal tissues.

### **Research control groups**

14. Control specimens, or subject control groups (patients) are used for research purposes. These can be control specimens to either run quality control (same as in diagnostic laboratories) or provide a reference point to analyze research data. The subject controls are usually groups of samples or individuals that are, by experiment design, accepted as a reference. Nature of these controls vary largely depending if the study is experimental (animals), clinical (patients treated prospectively), or descriptive (excision samples from patients). For example, for the first two scenarios individuals or animal are split into two groups: those who receive a treatment and those who receive a pseudotreatment (placebo). Then data are compared between the groups.

15. For descriptive studies, which encompass most of the pathology studies, a feature of interest can be described based on already established knowledge, as a lesion different from normal tissues (as in diagnostic work described above). This usually establishes the fact that a lesion can occur in patients with a specific history. Most lesions and abnormalities have been well described and their clinical implications are known. The novelty of these studies is mainly in a new setting or presentation. Publication of these studies enables pathologists to recognize the abnormality in cases with similar presentations. The feature can be studied further in detail comparing samples containing the lesion but from the patients with presentations or outcomes differing by a selected parameter. These studies are subject to validity of the controls since there may be no patients who are truly risk-free for the selected symptom or parameter. The symptoms may take time to develop (tissue taken before the symptoms became apparent), or are masked by confounding factors (patients do not feel pain due to nerve damage by other disease).

16. An example of the complex nature of pathology studies is the most common cause of death – heart attack. One of its most common finding at death is only partial occlusion of the heart vessels. In these sudden deaths, the tissues do not have time to develop vital reaction of ischemia in the heart and the only finding is partially occluded vessels. It is an established cause of death, but all people live with the occlusion to a certain point in time, many die from unrelated causes. Some people develop symptoms and live with the symptoms for many years, while for others cardiac death is the first symptom. In these complex cases, the connection between the cause and its manifestation is established by identification of the lesion, based on its difference from normal tissue, and exclusion of other lesions. For example, a partial occlusion of the vessels is not determined as a cause of death in a passenger sustaining a fatal trauma in a motor vehicle accident. However, the same finding can be determined as the cause of death in an individual with no other pathology sufficient to cause death.

17. The above example of partial arterial occlusion as a cause of death demonstrates that, for research projects, asymptomatic patients may not be used as a control group without a full understanding of the pathological processes. The aspects that need to be understood are: the time lag between the pathological change and the clinical symptoms (many diseases take years to become clinically apparent), and variability between patients (patients' bodies react differently to a causative agent and perception of the symptoms varies between patients).

18. In diagnostic work, pathologists rely on their knowledge of normal histology as a reference to detect abnormalities, established clinical effects of general (scarring, inflammation etc.) or specific (tumor type) pathological changes, exclusion of alternative possible pathological conditions, and correlation of the pathological analysis with the clinical findings (can the pathological findings explain clinical presentation?).

**Appropriate use of controls**

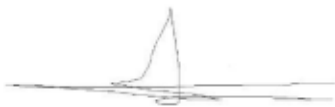
19. In my diagnostic and consult work I use histological features that are established as abnormal, or deviant from the normal range. They have been studied and described in the published literature. For example, in mesh samples I describe scarring and foreign body reaction. These features have been described and studied since the 19th century. I also describe nerves in the tissue as their function is also established, however I do not rely on nerve density in different mesh compartments which I currently investigate in my research. The former is subject to routine quality controls run at the laboratory, while the latter is investigated using research type of controls. For my research projects, I choose types of controls that are suitable for the type and the goals of the study.

20. Overall, as a trained physician, pathologist and scientist, I am well aware of the different types of controls and I use them appropriately.

21. I use the same approach to pathological and clinical analysis of patients in every case for this litigation, and that is also the same approach that I use when performing those same functions for cases that are outside of litigation.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed on April 27, 2017



---

Vladimir V. Iakovlev